

# HPTN 083 FAQ

## 1. What is HPTN 083?

HPTN 083 is the first study to compare the efficacy of a pre-exposure prophylaxis (PrEP) regimen consisting of a bi-monthly injection of long-acting cabotegravir (CAB LA) to daily oral tenofovir/emtricitabine (TDF/FTC) for HIV prevention. HPTN 083 enrolled 4,570 cisgender men and transgender women (TGW) who have sex with men at 43 sites in Argentina, Brazil, Peru, South Africa, Thailand, the United States, and Vietnam.



Cabotegravir Injection



Truvada Tablet

## 2. Why was this study being done?

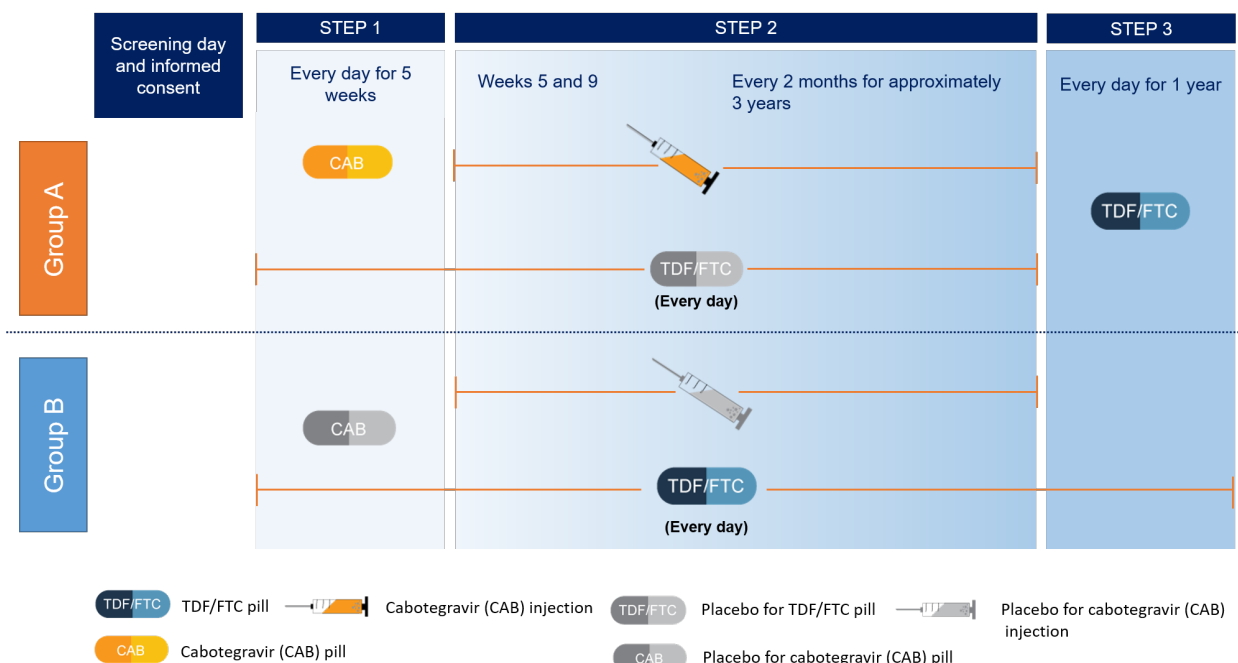
For many people, taking a daily pill can be challenging. The development of safe and effective long-acting alternative drugs for HIV PrEP would increase HIV prevention choices and help those who find taking a daily pill challenging. Some people also may find periodic injections to be a more discreet form of HIV PrEP than daily pills and may prefer long-acting injectable cabotegravir (CAB LA) for that reason.

## 3. What organizations are involved in HPTN 083?

The HPTN 083 study is conducted by the HIV Prevention Trials Network (HPTN) and sponsored by the U.S. National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. The study is jointly funded by NIAID and ViiV Healthcare. Study drugs are provided by ViiV Healthcare and Gilead Sciences, Inc.

## 4. What was the study design of HPTN 083?

Participants were assigned randomly (by chance) to either the CAB or oral TDF/FTC group. Neither the participants nor the study team knew who was in which group. Participants in each group received both injections and oral tablets – each participant received one active drug and one placebo (no active drug) in order to maintain the blinded nature of the study. Participants were randomized to one of two study arms and included three steps: Step 1 consisted of 5 weeks of daily oral CAB and a TDF/FTC placebo or 5 weeks of daily oral TDF/FTC and an oral CAB placebo; Step 2 consisted of 148 weeks of intramuscular CAB LA 600 mg every 8 weeks plus daily oral TDF/FTC placebo or 148 weeks of daily oral TDF/FTC plus an intramuscular CAB LA placebo every 8 weeks; and Step 3 consisted of an open-label daily oral TDF/FTC for 48 weeks after participants completed Step 2.



## 5. Why did the DSMB recommend stopping the blinded phase of the study?

On May 14, 2020, the independent Data and Safety Monitoring Board (DSMB) overseeing the study conducted a planned interim analysis of HPTN 083 study data and found that a regimen containing CAB LA injected once every 8 weeks safely and effectively prevented HIV acquisition in the study population. Consequently, the DSMB recommended that NIAID stop the blinded phase of the study and share the results. NIAID accepted the DSMB's recommendations, and preliminary findings were released on May 18, 2020 to serve the interests of public health.

## 6. What new information was presented at AIDS 2020?

After a more extensive analysis of the interim study data, the regimen containing CAB LA was found to be statistically superior to daily oral TDF/FTC for PrEP among the cisgender men and transgender women who have sex with men enrolled in HPTN 083. A total of 52 incident HIV infections occurred, with 13 incident infections in the CAB arm (incidence rate 0.41%) and 39 incident infections in the TDF/FTC arm (incidence rate 1.22%). The hazard ratio for the CAB versus TDF/FTC arms is 0.34 (95% CI 0.18-0.62), corresponding to a 66% reduction in incident HIV infections in study participants given CAB compared to TDF/FTC.

## 7. When the DSMB recommended stopping the trial, they noted that the study had crossed the stopping boundary for non-inferiority and was approaching the boundary for superiority. Why are the final findings now indicating that the regimen containing CAB-LA is superior to FTC/TDF?

The DSMB meeting on May 14, 2020, was the first formal efficacy review of data from HPTN 083. The criteria for stopping the trial early were specified to be extremely stringent, particularly at the first efficacy review, because the results would need to be strong enough to ensure HPTN 083 provided convincing evidence to support licensure of CAB LA for HIV prevention. During the May 14 meeting, the DSMB determined that the study had reached its objective – it exceeded the strength of evidence required to stop for non-inferiority at the first review.

Following the DSMB meeting, the HPTN evaluated the complete dataset using statistical methods that account for the fact that the study was stopped early based on the pre-specified interim monitoring plan. Based on this final analysis, the effect of CAB was determined to be HR=0.34 (adjusted 95% CI 0.18-0.62), which clearly excludes a HR of 1, meaning that CAB LA was superior to TDF/FTC ( $p=0.0005$ ) for prevention of HIV acquisition. The final statistical analysis was independently reviewed by statistical experts in the field of interim monitoring of clinical trials. The pharmaceutical companies played no role in the final analysis of data, which was overseen by the study sponsor NIAID.

## 8. Were the medications in the study deemed safe?

Both CAB and TDF/FTC were safe and generally well-tolerated. Participants receiving the regimen containing CAB LA were more likely to experience pain or tenderness at the injection site or a fever. Participants in the TDF/FTC group were more likely to report nausea.

## 9. What will happen to the participants in HPTN 083 now?

Study participants are being informed of the study results and of which medication they were receiving. Participants will be offered the opportunity to remain in the study, initially staying on the active study medication that they were assigned at the beginning of the study. Participants taking active TDF/FTC who wish to switch to the regimen containing CAB LA will be able to do so as soon as the medications are available. Participants may also continue taking daily oral TDF/FTC or switch to daily oral TDF/FTC if they do not want to take the regimen containing CAB LA anymore.

## 10. What were the study demographics?

Of the 4,566 participants that were part of this analysis, 67% were less than 30 years old, 12% were TGW, and 50% of the U.S. population self-identified as Black or African-American. Fifty-two incident HIV infections were observed overall.

## **11. Did participants who acquired HIV while taking the regimen containing CAB-LA have resistance identified in their HIV isolates?**

Resistance testing for all participants who acquired HIV in either arm of HPTN 083 is ongoing. As soon as those data are available, they will be presented and/or published in peer-reviewed settings.

## **12. Will the oral lead-in for CAB before receiving the first injection of CAB LA continue to be required?**

Initially, in HPTN 083's continuation, yes. The study will continue analyzing the safety data on the oral lead-in period of participants who switch from TDF/FTC to the regimen containing CAB LA. At the time of the release of study results in July 2020, discussions are going about the risks and benefits of an oral lead-in.

## **13. Was more information learned about the need for oral PrEP to “cover the tail” of participants who wish to stop receiving CAB LA?**

The study will continue collecting data on the specific case of participant who stop receiving injections of CAB LA. If a participant wants to stop receiving injections of CAB LA for PrEP and is still engaging in risk behaviors, they should transition to another HIV prevention modality - which may or may not include the use of a tenofovir-based PrEP product. In HPTN 083, participants will continue to be offered daily oral TDF/FTC for up to 48 weeks after their last CAB LA injection.

## **14. Is CAB also being tested for HIV prevention among cisgender women?**

Yes, a study called HPTN 084 is testing the safety and efficacy of CAB for HIV prevention among cisgender women. The study is taking place in sub-Saharan Africa and began in 2017. HPTN 084 was also reviewed by the DSMB, was recommended to continue, and will be continuously monitored by the same DSMB.

## **15. Why did the DSMB make this recommendation for HPTN 083 but decide HPTN 084 will continue?**

HPTN 084 began enrollment in November 2017, about a year after HPTN 083 began enrollment. There were not enough data available from HPTN 084 at the May DSMB meeting to determine if the study had reached its specified objectives. The DSMB will review data from HPTN 084 again later this year.

## **16. Did COVID-19 play a role in the recommendation of the DSMB?**

No. The data that the DSMB reviewed were almost entirely obtained prior to COVID-19-related disruptions at sites. However, due to the potential for COVID-19 to significantly disrupt the conduct and data integrity of HPTN 083 going forward, the DSMB did consider the potential effects of COVID-19 on the future of the study.

## **17. When will CAB LA be available for HIV PrEP?**

It is too early to know when CAB LA may be available for individuals outside the HPTN 083 study. The regulatory approval process for CAB LA requires several steps that need to occur first, including review and approval by the U.S. Food and Drug Administration and other regulatory agencies.